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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,423	11/13/2003	Hamdi K. Hamdi	HAMDI-001B	9959

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Matthew A. Newboles
STETINA BRUNDA GARRED & BRUCKER
75 Enterprise, Suite 250
Aliso Viejo, CA 92656

EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/712,423	HAMDI ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *12-14 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15 and 17-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/18/04, 2/23/04*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *2/21/06*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1-36 are pending of which claims 12-14 and 16 are withdrawn in this office action. Claims 1-11, 15 and 17-36 are rejected.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on February 18, 2004 and February 23, 2004 has been acknowledged.

Response to election Restriction

Claims 12-14, 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Further applicant elects formula II to be examined along with the election. Election was made **without** traverse in the reply filed on 27 March 2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1,2, 4, 7, 15 and dependent claims 9, 17-19 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear in the claim 1 from the claim language of "involves" treating a medical condition what would have been the medical condition that was treated that is affected by chemopreventive?

Claims 2 and 4 a pharmaceutical composition by default contains a "carrier" or "diluent" or else it would not be a composition thus it is not apparent how claim 2 is further limiting to claim 1.

Claims 3, 8, 11, 15 and 32 are also rejected under 35 U.S.C. 112, second paragraph, the claims contain language "effective amount" vague and indefinite and does not clearly specify what is meant by effective amount" as being effective for inhibition.

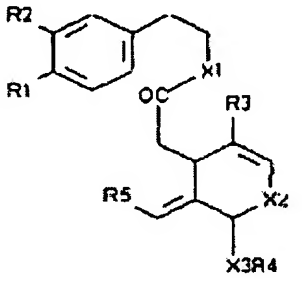
Claim Rejections - 35 USC § 112-first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

I. Claims 1, 7 and 11 together with dependent claims5, 9-10, 17-25, 29, 31 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting colon cancer cell migration *in vitro* and *in vitro* modulation of unregulated cell growth does not reasonably provide enablement for inhibiting colon cancer cell migration in invivo and invivo modulation of unregulated cell growth with the claimed compound. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims refer to "treating a medical condition" having chemopreventive activity with the compound



, based upon that, the applicant has not shown any invivo result to convey this. In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, 7) the relative skill of those skilled in the art and 8) the quantity of experimentation needed.

Rejection (based on the composition to treat any type of cancer)

1) Nature of the invention.

The nature of the invention is a method for treating a medical condition which involves cancer in a subject comprises administering the instant pharmaceutical composition to a patient (mammal) in need thereof. As stated, however, claims 1, 5, 10, 20, 24, 29, 31 and 35 recite that any medical conditions which involves cancer is intended.

2) State of the prior art and the predictability or lack thereof in the art.

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibited the desired pharmacological activities (i.e. what compounds can treat which specific disease eg., colon, breast, lung etc). The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between the claimed compound as capable of treating medical condition which involves inhibiting colon cancer cell migration, modulation of unregulated cell growth in vivo as well as in vitro, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of the claimed compound in vivo. Also Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first

and second para).

Also, more recently with regards to unpredictability, Johnson et al (British J. of Cancer 2001, 84(10) 1424-1431) teaches the use of 39 agents invivo activity in a particular histology in a tumor model did not closely relate to activity in the same human cancer. Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that the claimed compound composition could be predictably used as an anti-cancer agent for any type of medical conditions which involves cancer as inferred by the claim and as contemplated by the specification. Further, the refractory nature of cancer to drugs is well known in the art

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would first need to determine the type of cancer to be treated, and then determine what dosage of the claimed compounds would be suitable for said treatment and/or prevention without toxicity to the patient in need thereof. Guru et al taken with Johnson et al (cited above makes it clear that much more than routine experimentation is needed).

4) Level of predictability in the art.

The art pertaining to the treatment of a/any medical condition which involves cancer remain highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art. Firstly, the mode of action in vitro is different from the mode of action invivo. Even within the animal models, a compound effective against cancer or a disease associated with cancer with

a positive result in an animal model does not necessarily mean a positive result in humans. Cancer is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the cancer reaction. There is no common mechanism by which any, or even most, cancer arise.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is no where found in the specification. However, the gap between *in vitro* activity and *in vivo* utility is large enough to warrant thorough and compelling *in vivo* or clinical data.

6) Existence of working examples.

As discussed above, no working example is found in the current application. Applicant's omission of working examples does not enable one of ordinary skill in the art to treat all cancers encompassed by the instant invention.

7) Breadth of claims.

Claims 1, 5, 10, 20, 24, 29, 31 and 35 are extremely broad due to the recitation of all types and forms of cancer encompassed by the instant invention.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of any disease. As a result necessitating

one of ordinary skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

II. **Rejection based on treating any type of cancer with one compound.**

1) The nature of the invention: The nature of the invention is treating all medical conditions associated with cancers which is extremely broad. For example pancreatic cancer, there is hardly a cure for this type of cancer. In view of the report Pancreatic cancer 2006, 90% of patients die within 12 months of diagnosis.

2) The state of the prior art: There are no examples shown in the specification on how to treat any medical conditions associated with cancer using the compound invivo. The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which cancer cell was inhibited by the compound. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting an invitro regime on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between treating conditions of any-type of cancer, one of skill in the art is unable to fully predict possible results from the administration of the compound due to the unpredictability of the role of the diseases.

3) The predictability or lack thereof in the art: there is currently no completely effective therapy for treating a genus medical condition which are cancer, with one compound. Search for therapeutic agents useful for the treatment of cancer is ongoing. For example: The art pertaining to the treatment of cancer of any type of cancer remain highly unpredictable because there is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the disease.

4) The amount of direction or guidance present -The specification only provides examples to treating colon cell (invitro) and wounds (invitro). While the invitro examples may suffice as a preliminary step into the research, it no-where shows how one can extrapolate the date to an invivo testing. The examples shown will not enable one skilled in the art to treat any types of cancerous diseases.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present found on pages 20-26 is not sufficient to enable one of skill in the art to treat all medical conditions that are cancers in vivo which embraces a myriad of conditions

6) Existence of working examples.

As discussed above, the working examples are found on pages 20-26 are insufficient for such a broad claim of treatment of all disease of angiogenesis. Applicant's limited working example does not enable one of ordinary skill in the art to treat all medical conditions which are cancer in the instant invention.

7) Breadth of claims.

Claim 1 is extremely broad due to the recitation of all types and forms of cancer encompassed by the instant invention.

8) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which cancers exhibit inhibitory effect of the instantly claimed compound.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of all cancers. As a result necessitating one of skill in the art to perform an exhaustive search to determine which diseases can be treated by the compound(s) of the instant claims in order to practice the claimed invention.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms, and treatment (or lack thereof) for cancer.

I. Claims 1, 3,11 and 15 together with dependent claims 2, 4-6, 9, 17-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in

possession of the claimed invention. There is no description in the specification for treatment of a representative types of cancers listed in the above claims.

Double Patenting

I. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

I. Claims 1-11, 15, and 17-36 are rejected on the ground of nonstatutory double patenting over claims 1-30 of U. S. Patent No. 6,632,798 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: treating medical condition. It is obvious that angiogenesis performs a critical role in the development of cancer. New blood vessel development is an important process in tumor progression. It favors the transition from hyperplasia to neoplasia i.e. the passage from a state of cellular multiplication to a state of uncontrolled proliferation characteristic of tumor cells, thus making the subject matter, treating medical condition in the current claim overlapping with the patented claims.

Both sets of claims refer to treating a medical condition by administering a pharmaceutical composition having chemopreventive activity, in an effective amount in the current application (claims 1-11, 15 and 17-36) refers to treating a medical condition (cancer) and (claims 1-10 refers to angiogenesis) claims 11-14 refers to cancer) and (15-30) in the patent refers to treating conditions which involves angiogenesis and cancer. With regards to the “effective amount” the instant claims are not limited to cancer due to the unclarity of what the method is effective for-thus any medical

condition that is given any amount is effective. The current application claims are an obvious variation of the copending application claims because:

Both set of claims recite using the same compositions and/or derivatives thereof for treating medical condition. See current application claims 1-11, 15 and 17-36 and patent claims 1 -30. The compositions recited in claims 1- 36 of the current application are an obvious variation of claims 1- 30 in the patent claims.

In view of the foregoing, the patent application claims and the current application claims are obvious variations.

II. Claims 1-11, 15, and 17-36 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-30 of the co-pending application 10/657,414. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows: The subject matter claimed in the instant application is fully disclosed in the co-pending application. It is obvious that angiogenesis performs a critical role in the development of cancer. New blood vessel development is an important process in tumor progression. It favors the transition from hyperplasia to neoplasia i.e. the passage from a state of cellular multiplication to a state of uncontrolled proliferation characteristic of tumor cells, thus making the subject matter, treating medical condition in the current claim overlapping with the patented claims.

Both sets of claims refer to treating a medical condition cancer in the instant claim application (claims 1-11, 15, and 17-36) and in the copending application – an angiogenesis related disease in the current application (1-30) with the same identical

compound. The current application claims anticipate the copending application claims because cancer is a medical disease/condition that results from angiogenesis.

Both applications recite using the same compositions and/or derivatives thereof. See current application claims 1-11, 15, and 17-36 and copending application claims 1-30. The compositions recited in the claims are anticipatory of each other. With regards to the "effective amount" the instant claims are not limited to cancer due to the unclarity of what the method is effective for-thus any medical condition that is given any amount is effective.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ardin H. Marschel 6/11/06

SVG
5/19/09

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER